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| APPLICATION NO.                 | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---------------------------------|-------------|----------------------|---------------------|------------------|
| 10/001,684                      | 10/25/2001  | David P. Katz        | AMBIINC.006A        | 3175             |
| 20995                           | 7590        | 05/18/2004           | EXAMINER            |                  |
| KNOBBE MARTENS OLSON & BEAR LLP |             |                      | LEITH, PATRICIA A   |                  |
| 2040 MAIN STREET                |             |                      | ART UNIT            |                  |
| FOURTEENTH FLOOR                |             |                      | PAPER NUMBER        |                  |
| IRVINE, CA 92614                |             |                      | 1654                |                  |

DATE MAILED: 05/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

|                              |                        |                     |  |
|------------------------------|------------------------|---------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b> | <b>Applicant(s)</b> |  |
|                              | 10/001,684             | KATZ, DAVID P.      |  |
|                              | <b>Examiner</b>        | <b>Art Unit</b>     |  |
|                              | Patricia Leith         | 1654                |  |

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☒ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-25 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-25 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                        | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. ____.  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date ____.   | 6) <input type="checkbox"/> Other: ____.                                    |

Art Unit: 1654

### **DETAILED ACTION**

Claims 1-25 are pending in the application and were examined on the merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a previous Office Action.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Specifically, claim 1 newly recites 'wherein said chromium-containing compound is not chromium yeast'. Support for this negative limitation cannot be found in the Instant specification as filed. Furthermore, the term 'chromium complexes' is defined as

Art Unit: 1654

specifically including chromium yeast [0042]. Thus, it is deemed that the Instant specification as filed does not support this new negative limitation. This new limitation is deemed new matter because it cannot be found in the Instant Specification where Applicants reduced to practice or even contemplated the scope of the claims.

It is noted that for purposes of applying prior art, the claims have been treated on the merits as they stand, including the new limitation which constitutes New Matter.

***Claim Rejections - 35 USC § 103***

Claims 1-25 remain rejected, under 35 U.S.C. 103(a) as being unpatentable over de la Harpe et al. (US 5,980,905) in view of Ostlund et al. (US 5,550,166) for the reasons set forth on the record.

Applicant's arguments as well as the Declaration filed under 37 CFR 1.132 were fully considered but not found convincing.

Declarant's qualifications and expertise are duly noted. Declarant refers to Exhibit B, an internet reference which details an NIH pilot study evaluating the effects of chromium picolinate on PCOS patients. Declarant states:

"PCOS is a little-understood condition that is the leading cause of infertility. At present there is no FDA-approved drug specifically designed to treat PCOS. While some doctors prescribe insulin-

Art Unit: 1654

sensitizing agents including metformin, these agents have been associated with undesirable side effects including nausea, diarrhea and loss of appetite. While decreased insulin sensitivity is associated with PCOS, this is a complex multifaceted disease. There is substantial uncertainty regarding its causes and treatments, and as such, it is not possible to predict with any level of confidence whether any particular agent, untested in this disease, would or would not have a beneficial effect" (paragraph 8, Affidavit)".

This statement is not without merit. However, it is reiterated that insulin resistance is one of numerous etiologies associated with PCOS. Although the Instant claims state 'treating PCOS' it is understood that what is actually being treated is insulin resistance as indicated by the Instant specification. Declarant states that 'PCOS is a multifaceted disease..There is substantial uncertainty regarding its causes and treatments...'. However, again, it is reiterated that insulin resistance was a known symptom of PCOS. Therefore, the ordinary artisan would have had a reasonable expectation that an agent which was known to alleviate insulin resistance; i.e., facilitate insulin's functions, would have treated insulin resistance and thereby offered some beneficial treatment for PCOS or any disease whereby a symptom of the disease was insulin resistance. This is especially in light of the fact that PCOS patients were taking medications such as metformin for decreasing insulin resistance as stated by Declarant.

Thus, although PCOS itself may be a multifaceted disease with no known origin, it is well accepted in the medical art that if the causative factors of a disease are unknown, the symptoms of the disease are none-the-less treated. For example, it

Art Unit: 1654

would be obvious to treat a fever in a patient with aspirin, even though the causative factors of the fever were unknown.

It is deemed that the Affidavit does not demonstratively evidence that the ordinary artisan would not have any reasonable expectation that chromium picolinate, which was known for lowering blood glucose levels in individuals as well as decreasing insulin resistance, would have been an advantageous treatment of PCOS.

Although the Affidavit indicates that insulin sensitivity was significantly increased, it remains deemed that this is an expected result since the prior art taught that chromium decreased insulin resistance.

Applicant's arguments were also fully considered, however, not found persuasive.

Applicant argues that "The mere fact that the teachings of de la Harpe et al. and Ostlund et al. might be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the composition' (*In re Mills*, cited on p.7-Arguments). "Both references are completely silent with respect to the benefits of administering a chromium complex for ameliorating the symptoms associated with PCOS because neither reference appreciated that chromium...affected symptoms of PCOS such as insulin resistance". Applicant further contends that the

Art Unit: 1654

Examiner is making 'hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention' (*In re Fine*, p. 8-Arguments). "Contrary to the position taken by the Examiner neither the '905 reference nor the '166 reference teach or suggest a relationship between chromium supplementation and the alleviation of insulin resistance" (p. 8-Arguments).

These arguments are not convincing for the following reasons:

Although de la Harpe et al. did not *explicitly* use the term 'Insulin resistance', one of ordinary skill in the art would have understood that when they stated 'Chromium functions as a cofactor for insulin. It binds to the insulin receptor and potentates many, and perhaps all of its functions" , that chromium decreases insulin resistance which is characterized by decrease of insulin receptor function. de la Harpe et al. did not need to specifically state the term 'insulin resistance' in order to clearly convey the effect of chromium administration to the ordinary artisan.

Ostlund et al. clearly taught that PCOS was a disease characterized, in part, by insulin resistance, and offered compositions effective in alleviating insulin resistance to treat diseases such as PCOS which were associated with insulin resistance. de la Harpe et al. taught that chromium alleviated insulin resistance. Therefore, one of ordinary skill in the art would have been motivated to treat PCOS with chromium compounds, such as chromium picolinate, because chromium was known to decrease

Art Unit: 1654

insulin resistance (as disclosed by de la Harpe et al.) and insulin resistance was a known symptom of PCOS as disclosed by Ostlund et al. The ordinary artisan would have had a reasonable expectation that chromium compounds including chromium picolinate would have had a positive effect on decreasing insulin resistance, because chromium was known to decrease insulin resistance according to de la Harpe (again, it is reiterated that although de la Harpe et al. did not explicitly recite 'insulin resistance' they explained the mechanism of chromium compounds in *sufficient detail* to allow one of ordinary skill in the art to understand that chromium compounds potentate the action of insulin).

Applicants argue that 'it is not reasonable to expect that an essential metal such as chromium as described in the de la Harpe et al. reference could be substituted for a carbohydrate such as pinitol...' (p. 8- Arguments). Applicant further argues that Ostlund et al. did not provide any clinical data with regard to pinitol and the treatment of PCOS and that PCOS is part of a laundry list of diseases in which insulin sensitivity is compromised. It is pointed out that although PCOS was one of many diseases listed which were associated with insulin resistance, the fact that PCOS was associated with insulin resistance was nevertheless disclosed and known in the prior art. Further, the Examiner did not base this rejection upon the suitable substitution qualities of pinitol and chromium. As stated *supra*, Ostlund et al. taught that PCOS was associated with insulin resistance and de la Harpe et al. taught that insulin resistance was alleviated with chromium which thereby led to improved glucose leveled (lowered). It would

Art Unit: 1654

therefore been *prima facie* obvious to treat PCOS with an agent which was known to improve insulin resistance such as chromium, in the form of chromium picolinate.

Applicant argues that de la Harpe et al. did not teach administration of chromium compounds to individuals with PCOS (p. 10 – Arguments). The examiner recognizes that obviousness can only be established by *combining or modifying* the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the ordinary artisan would have been motivated to administer a chromium compound such as chromium tripicolinate to a person suffering from PCOS because PCOS was known to be characterized in part by insulin resistance as taught by Ostlund et al. and because chromium compounds such as chromium tripicolinate were known to decrease insulin resistance as taught by de la Harpe et al.

Thus, the rejections stand.

No Claims are allowed.

Art Unit: 1654

***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia Leith whose telephone number is (571) 272-0968. The examiner can normally be reached on 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0968. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Art Unit: 1654

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patricia Leith  
Primary Examiner  
Art Unit 1654

05/13/04

A handwritten signature in black ink that reads "Patricia Leith". The signature is written in a cursive, flowing style with a large initial "P".

**PATRICIA LEITH  
PRIMARY EXAMINER**